
Mrc1 and DNA polymerase epsilon function together in linking DNA replication and the S phase checkpoint.

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Public Summary:

Scientific Abstract:

Yeast Mrc1, ortholog of metazoan Claspin, is both a central component of normal DNA replication forks and a mediator of the S phase checkpoint. We report that Mrc1 interacts with Pol2, the catalytic subunit of DNA polymerase epsilon, essential for leading-strand DNA replication and for the checkpoint. In unperturbed cells, Mrc1 interacts independently with both the N-terminal and C-terminal halves of Pol2 (Pol2N and Pol2C). Strikingly, phosphorylation of Mrc1 during the S phase checkpoint abolishes Pol2N binding, but not Pol2C interaction. Mrc1 is required to stabilize Pol2 at replication forks stalled in HU. The bimodal Mrc1/Pol2 interaction may be an additional step in regulating the S phase checkpoint response to DNA damage on the leading strand. We propose that Mrc1, which also interacts with the MCMs, may modulate coupling of polymerization and unwinding at the replication fork.

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